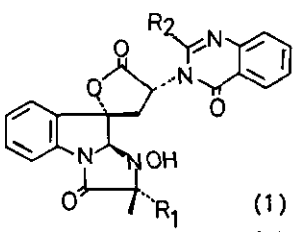
THE SYNTHETIC STUDIES ON TRYPTOQUIVALINES AND THE RELATED COMPOUNDS
A FORMAL TOTAL SYNTHESIS OF (±)-TRYPTOQUIVALINE G

Takeshi Ohnuma, Youichi Kimura, Hitoshi Kasuya, and Yoshio Ban
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060 Japan

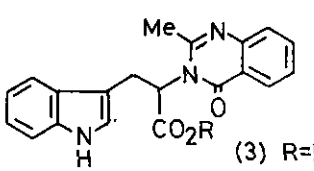
A strain of the fungus *Aspergillus clavatus* collected from mold damaged rice produced a group of toxic, tremor inducing metabolites of novel structures. Tryptoquivaline (1) was found to be the major metabolites, which are tetrapeptides derived from four amino acids including tryptophan. Tryptoquivaline G (2) is a representative of a more recently discovered group of mycotoxins produced by *Aspergillus fumigatus*.

We attempted to synthesize these unique metabolites by means of the new oxidation method of the suitable tryptophan derivatives with thallium trinitrate (TTN), developed by us. Oxidation of indole-3-propionic acid with TTN in 10% aq.CH_3CN could be converted in one pot to oxindole-3-propionic acid lactone.

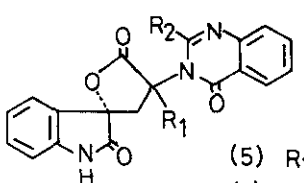
Tryptophan derivative (3) was synthesized by reaction of L-tryptophan methylester and acetyl anthranilic acid with phosphorous trichrolide. Hydrolysis of (3) with lithium hydroxide yielded racemic carboxylic acid (4). Oxidation of (4) with TTN in aq.CH_3CN-DMF gave oxindole-3-propionic acid lactone (5 and 6). Oxidative removal of methyl group of (5) with SeO_2 in glc.acetic acid at reflux afforded lactone (7),which is the intermediate of Buchi's tryptoquivaline G synthesis.



(1) R_1=Me R_2= 
(2) R_1=Me R_2= H



(3) R=Me
(4) R=H



(5) R_1= α-H R_2=Me
(6) R_1= β-H R_2=Me
(7) R_1=α-H R_2=H